REMARKS

This is a response to the Office Action mailed February 6, 2003. Claims 1-3, 5-7, 10-32, 37-39, 41-44 and 46-72 are pending in the application. Claims 1-3, 5-7, 9-32, 37-39 and 41-44 have been rejected by the Examiner. As noted above, Applicants have canceled Claims 4, 8, 9, 33-36, 40 and 45 without prejudice, amended Claims 1-3, 6, 7, 13-16, 18, 20-23, 30-32, 37-39, 42 and 44 and submitted new Claims 46-72. The amendments and the New Claims 46-72 are fully supported by the written description. Also, no new matter has been introduced into the application.

Election/Restrictions/Response to Applicants' Election

Applicants affirm election of Claims 1-3, 5-7, 9-32, 37-39 and 41-44. Applicants have canceled Claims 4, 8, 33-36, 40 and 45 without prejudice.

Claim Rejections – 35 U.S.C. § 102

The Examiner has rejected Claims 1-3, 5-7, 9-16, 21-32 and 37-39 under 35 U.S.C. §102(e) as being anticipated by Turnlund et al. (US 2001/0001806A1). Turnlund et al. is directed to a method for increasing the rate of thrombus formation and/or proliferative cell growth of a selected region of cellular tissue by endovascularly irradiating the selected region with radiation (see abstract). According to Turnlund et al., "[p]referably, the delivery means includes a deformable endovascular prosthesis (25) adapted for secured positioning adjacent to the selected region (21) of cellular tissue (22), and a radioactive source" (abstract). Turnlund et al. disclose that a stent graft can be "constructed to deliver a dose of endovascular radiation upon the selected region 21 (i.e., the arterial wall of the aneurysmal sac 27 that is formed between the stent graft and the wall of the blood vessel), while maintaining vessel patency" (page 4, paragraph 40). Turnlund et al. further disclose that "to limit potentially occlusive in-growth at

the proximal and distal ends of stent graft 23, the proximal and distal end portions of the stent which anchor the stent to the vessel may have different activities as compared to the growth inducing radioactivity of the central portion 38 of the stent (FIG. 8)" (page 6, paragraph 57).

According to the Federal Circuit, "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631 (Fed. Cir. 1987). Turnlund et al. clearly fail to disclose all of the limitations of the claimed invention. For instance, Turnlund et al. fail to disclose an apparatus for delivering a therapeutic agent to a vessel, including "an elongated source of a therapeutic agent, **the source having gradients of therapeutic agent concentrations along a length of the elongated source near a proximal end and a distal end of the elongated source**" as recited by amended Claim 1. Although Turnlund et al. disclose a stent with proximal and distal end portions that can have "**different activities**" as compared to the central portion of the stent, Turnlund et al. absolutely do not disclose a stent that has **gradients of therapeutic agent concentrations**. In other words, in stark contrast to Claim 1 of the present invention, Turnlund et al. clearly do not disclose a stent with a portion having a gradually or incrementally changing concentration of a therapeutic agent over a length of the stent.[1] The disclosure of having "different activities" simply does not mean that the concentration is gradually varying along the length of the device.

Furthermore, referring to Claim 2, Turnlund et al. do not disclose gradients that comprise "therapeutic agent concentrations **gradually decreasing along the length of the elongated source**." Turnlund et al. specifically do not disclose that the activity of the stent can "**gradually decrease**" as claimed by amended Claim 2.

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[1] It appears from the Office Action that the Examiner is suggesting that Figure 6 of Turnlund et al. shows that a stent can have proximal and distal end portions that have "different activities" as compared to the central portion of the stent. Applicants disagree. Figure 6 only provides a illustration of the dose provided by the stent at a distance

Turnlund et al. also fail to disclose at least some of the limitations of the other independent claims. For example, Turnlund et al. at least fail to disclose an apparatus including "**a region of a radioactivity gradient** transitioning from the therapeutic level to a non-therapeutic level of radioactivity" as recited by amended Claim 6; an intravascular stent having "**radioactivity gradients** near a proximal end and a distal end of the radioactive region" as recited by amended Claim 21; or an intravascular stent having "**drug concentration gradients** near a proximal end and a distal end of the stent" as recited by amended Claim 31. Additionally, Turnlund et al. at least fail to disclose a method of producing a radioactive delivery source that includes "forming **radioactivity gradients** within the radioactive region near the proximal end and the distal end of the region" as recited by amended Claim 13, and a method of producing a drug source that includes "forming **drug concentration gradients** within the drug region near the proximal end and the distal end of the drug region" as recited by amended Claim 37.

Because it appears that the Examiner has completely ignored many of the limitations of the claimed invention, Applicants respectfully request the Examiner to reconsider the Section 102(e) rejection and allow Claims 1-3, 5-7, 10-16, 21-32 and 37-39. Claim 9 has been canceled without prejudice.

Claim Rejections – 35 U.S.C. § 103

The Examiner has rejected Claims 17-20 and 41-44 under 35 U.S.C. §103(a) as being unpatentable over Turnlund et al. As noted above, Claim 13 is allowable over Turnlund et al. Claims 17-20 depend directly or indirectly from Claim 13, and are allowable for at least the same reason. Additionally, as shown above, Claim 37 is allowable over Turnlund et al. Claims 41-44 depend directly or indirectly from Claim 37, and are allowable for at least the same reason.

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away from the stent, and hence does not provide information on the concentration of radioactivity on the stent structure.

CONCLUSION

Claims 1-3, 5-7, 10-32, 37-39, 41-44 and 46-72 are pending in this application. Examination and allowance of the claims are respectfully requested. If the Examiner has any questions or concerns, the Examiner is invited to telephone the undersigned attorney at (415) 954-0345.

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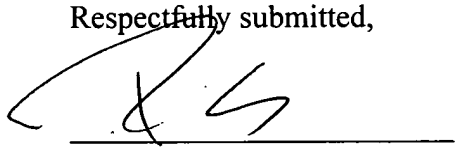
Respectfully submitted,



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Version With Markings To Show Changes Made

IN THE CLAIMS

Claims 4, 8, 9, 33-36, 40 and 45 have been canceled without prejudice. Claims 1, 2, 6, 7, 13-16, 18, 20-23, 30-32, 37-39, 42 and 44 have been amended. New claims 46-73 have been added. The italicized claims are the remaining claims which have not been amended in this Response and are provided for the Examiner's reading convenience. Please amend the claims as indicated below:

1. (Amended) An apparatus **to deliver a therapeutic agent to a vessel**, comprising:

an elongated source of a therapeutic agent ~~to deliver a dose of the therapeutic agent to a vessel~~, the source having gradients of therapeutic agent concentrations **along a length of the elongated source** near a proximal end and a distal end of the elongated source.

2. (Amended) The apparatus of claim 1 wherein the gradients comprise therapeutic agent concentrations gradually decreasing ~~near~~**along** the ~~proximal end and the distal end~~**length** of the elongated source.

3. (Amended) The apparatus of claim 1 wherein the source comprises a radioactive intravascular stent **or a drug eluting stent**.

Please cancel Claim 4.

5. *The apparatus of claim 1 wherein the source comprises a drug delivery stent having an anti-cell proliferation drug for treatment of the vessel.*

6. (Amended) An apparatus **for delivering therapeutic radiation to a vessel**, comprising:

an elongated radiation ~~dose~~ delivery source ~~having~~**including** a radioactive region thereon, the radioactive region having a proximal end and a distal end, **and being capable of delivering** a

therapeutic **level of** radioactivity ~~**level between the proximal end and the distal end**~~, **wherein** the radioactive region ~~**also having regions of radioactivity gradients**~~**includes a region of a radioactive gradient** ~~**to transition**~~**transitioning** from the therapeutic ~~**radioactivity**~~ level to a non-therapeutic **level of** radioactivity ~~**level**~~ near the proximal end and the distal end **of the radioactive region**.

7. (Amended) The apparatus of claim 6 wherein the radiation ~~**dose**~~ delivery source comprises an intravascular stent.

Please cancel Claims 8 and 9.

10. *The apparatus of claim 6 wherein the radioactive region comprises a beta particle emitting isotope.*

11. *The apparatus of claim 6 wherein the radioactive region comprises a gamma particle emitting isotope.*

12. *The apparatus of claim 6 wherein the radioactive region comprises a beta particle and a gamma particle emitting isotope.*

13. (Amended) A method **of producing a radioactive delivery source**, comprising:

~~**providing an elongated radiation dose delivery source;**~~

forming a radioactive region on ~~**the**~~**a radioactive** delivery source, the radioactive region having a proximal end and a distal end, **and being capable of delivering** a therapeutic **level of** radioactivity ~~**level**~~ between the proximal end and the distal end; and

forming ~~**regions of**~~ radioactivity gradients ~~**on**~~**within** the radioactive region near the proximal end and the distal end **of the region**, the radioactivity gradients transitioning from the therapeutic **level of** radioactivity ~~**level**~~ to a non-therapeutic **level of** radioactivity ~~**level**~~.

14. (Amended) The method of claim 13 wherein forming the ~~**regions of**~~ radioactivity gradients comprises uniformly decreasing the radioactivity level from the therapeutic level to the non-therapeutic level.

15. (Amended) The method of claim 13 wherein forming the ~~regions of~~ radioactivity gradients comprises variably decreasing the radioactivity level from the therapeutic level to the non-therapeutic level.

16. (Amended) The method of claim 13 wherein forming the ~~regions of~~ radioactivity gradients comprises decreasing the radioactivity level by incremental steps from the therapeutic level to the non-therapeutic level.

17. *The method of claim 13 wherein forming the radioactive region comprises coating the delivery source with isotopes by ion beam implantation.*

18. (Amended) The method of claim 17 wherein forming the ~~regions of~~ radioactivity gradients ~~on the radioactive region~~ comprises gradually decreasing an ion beaming time.

19. *The method of claim 13 wherein forming the radioactive region comprises coating the delivery source with isotopes by plasma implantation.*

20. (Amended) The method of claim 19 wherein forming the ~~regions of~~ radioactivity gradients ~~on the radioactive region~~ comprises masking the proximal end and the distal end of the radioactive region with radioactivity shields.

21. (Amended) An intravascular stent **for delivering therapeutic radiation to a vessel**, comprising:

a radioactive region along an elongated length of ~~the~~**a** stent ~~to deliver a radiation dose to a vessel wall~~, the radioactive region having an area **capable** of **delivering a** substantially uniform ~~radioactivity level to provide a therapeutic~~ dose **of radioactivity** to ~~the~~**a** vessel ~~wall, the uniform radioactivity level~~ localized near a central portion of the stent, **wherein** the radioactive region ~~also having~~**includes** radioactivity ~~level~~ gradients near a proximal end and a distal end of the ~~stent~~**radioactive region**, the radioactivity ~~level~~ gradients ~~to decrease~~ gradually **decreasing** the dose delivered to the vessel ~~wall~~ from ~~the~~**a** therapeutic ~~dose~~ level to a non-therapeutic ~~dose~~ level **of radioactivity**, **and wherein** the gradients ~~to~~ decrease **the dose** from a

point inward of the proximal end to or near the proximal end, and ~~to~~ decrease **the dose** from a point inward of the distal end to or near the distal end of the radioactive region.

22. (Amended) The stent of claim 21 wherein the radiation dose delivered to the vessel ~~wall~~ inhibits vessel cell proliferation along the elongated length of the stent and past the proximal end and the distal end of the stent.

23. (Amended) The stent of claim 21 wherein the area **capable** of **delivering the** substantially uniform **level of** radioactivity ~~level~~ comprises a greater longitudinal length than each of the gradients.

24. *The stent of claim 21 wherein the gradients comprise a uniform rate of decrease of radioactively level.*

25. *The stent of claim 21 wherein the gradients comprise a variable rate of decrease of radioactivity level.*

26. *The stent of claim 21 wherein the gradients comprise a decrease of radioactivity level by incremental steps.*

27. *The stent of claim 21 wherein the radioactive region comprises a beta particle emitting isotope.*

28. *The stent of claim 21 wherein the radioactive region comprises a gamma particle emitting isotope.*

29. *The stent of claim 21 wherein the radioactive region comprises a beta and a gamma emitting particle isotope.*

30. (Amended) The stent of claim 21 wherein the ~~radiation~~ dose **of radioactivity** comprises up to 60 Gray.

31. (Amended) An intravascular stent **for delivering a drug to a vessel**, comprising:

a drug delivery region along a surface of an elongated length of ~~the~~**a** stent, the drug delivery region having a variable drug concentration thereon ~~to deliver a drug dose to a vessel~~

~~wall~~, **wherein** the drug delivery region ~~having~~**includes** an area of substantially uniform drug concentration ~~to provide a therapeutic dose to the vessel wall, the substantially uniform drug concentration~~ localized near a central portion of the stent, **and wherein** the drug delivery region ~~also having~~**includes** drug concentration gradients near a proximal end and a distal end of the stent, the drug concentration gradients ~~to decrease~~ gradually **decreasing** ~~the dose delivered to the vessel wall~~ from ~~the~~**a** therapeutic dose level to a non-therapeutic dose level, **and wherein** the gradients ~~to~~ decrease from a point inward of the proximal end to or near the proximal end, and ~~to~~ decrease from a point inward of the distal end to or near the distal end of the drug delivery region.

32. (Amended) The stent of claim 31 wherein the drug dose delivered to the vessel ~~wall~~ inhibits vessel cell proliferation along the elongated length of the stent and past the proximal end and the distal end of the stent.

Please cancel Claims 33-36.

37. (Amended) A method **of producing a drug source**, comprising:

~~providing an elongated, intravascular drug source;~~

forming a drug region on ~~the~~**a** drug source, the drug region having a proximal end and a distal end, **and having** a therapeutic **level of** drug concentration ~~level~~ between the proximal end and the distal end; and

forming ~~regions of~~ drug concentration gradients ~~on~~**within** the drug region near the proximal end and the distal end **of the drug region**, the concentration gradients transitioning **the drug concentration** from the therapeutic **level of** drug concentration ~~level~~ to a non-therapeutic **level of** drug concentration ~~level~~.

38. (Amended) The method of claim 37 wherein forming the ~~regions of~~ drug concentration gradients ~~comprises~~**within the drug region comprise** uniformly decreasing the drug concentration ~~level~~ from the therapeutic level to the non-therapeutic level.

39. (Amended) The method of claim 37 wherein forming the ~~regions of~~ drug concentration gradients ~~comprises~~**within the drug region comprises** variably decreasing the drug concentration ~~level~~ from the therapeutic level to the non-therapeutic level.

Please cancel Claim 40.

41. *The method of claim 37 wherein forming the drug region comprises dipping the drug source in a drug.*

42. (Amended) The method of claim 41 wherein forming the ~~regions of~~ drug concentration gradients ~~on~~**within** the drug region comprises masking the proximal end and the distal end **of the drug region**.

43. *The method of claim 37 wherein forming the drug region comprises coating the drug source with a drug.*

44. (Amended) The method of claim 43 wherein forming the ~~regions of~~ drug concentrations gradients ~~on~~**within** the drug region comprises varying a translational drug spraying speed.

Please cancel Claim 45.

Please add the following new claims:

46. (New) A stent to deliver a therapeutic agent to a biological lumen, comprising a body and a therapeutic agent deposited on the body of the stent, wherein the concentration or amount of therapeutic agent gradually changes along a length of the stent.

47. (New) The stent of Claim 46, wherein the therapeutic agent is a radioactive substance.

48. (New) The stent of Claim 46, wherein the therapeutic agent is a drug.

49. (New) The stent of Claim 48, wherein the drug is disposed in a polymeric coating.

50. (New) The stent of Claim 46, wherein the concentration or amount of therapeutic agent gradually decreases from an area within a middle segment of the stent towards an end of the stent.

51. (New) The stent of Claim 46, wherein the concentration or amount of therapeutic agent changes at a constant rate along the length of the stent.

52. (New) The stent of Claim 46, wherein the concentration or amount of therapeutic agent changes incrementally along the length of the stent.

53. (New) A method of producing a stent, comprising depositing a therapeutic agent onto a body of a stent, wherein the amount or concentration of the therapeutic agent deposited onto the body gradually changes along a length of the stent.

54. (New) The method of Claim 53, wherein the therapeutic agent is a radioactive substance.

55. (New) The method of Claim 53, wherein the therapeutic agent is a drug.

56. (New) The method of Claim 53, wherein the drug is disposed in a polymeric coating.

57. (New) The method of Claim 53, wherein the length is a segment of the stent in close proximity to one end of the stent.

58. (New) The method of Claim 53, wherein the length is defined as any segment along a longitudinal length of the stent.

59. (New) The method of Claim 53, wherein the therapeutic agent is deposited so that the concentration or amount gradually decreases from an area within a middle segment of the stent towards an end of the stent.

60. (New) The method of Claim 53, wherein the therapeutic agent is deposited so that the concentration or amount changes at a constant rate along the length of the stent.

61. (New) The method of Claim 53, wherein the therapeutic agent is disposed in a polymeric coating and the length is defined as any segment of the coating extending longitudinally from a first segment of the stent to a second segment of the stent.

62. (New) The method of Claim 53, wherein the therapeutic agent is deposited so that the concentration or amount changes in incremental segments along the length of the stent.

63. (New) A drug eluting stent, comprising:

a body having a first end and a second end and a middle segment between the first and second ends; and

a drug deposited on the stent, wherein the middle segment of the stent has more of the drug than the first or second end of the stent.

64. (New) The stent of claim 63, wherein the drug is deposited in a polymeric coating.

65. (New) A drug eluting stent, comprising:

a body having a first end and a second end and a middle segment between the first and second ends; and

a drug deposited along the middle segment of the stent, wherein the first or second end of the stent is free from any drug.

66. (New) The stent of Claim 65, wherein one of the first or second ends includes a drug deposited thereon.

67. (New) A stent comprising a body having a first end, a second end and a middle segment, wherein a concentration of a drug carried by the stent is greater at the middle segment of the stent as compared to the first or second end.

68. (New) The stent of claim 67, wherein the drug is carried by a polymeric coating.

69. (New) A method of forming a coating on a stent, the stent comprising a body having a first end, a second end and a middle segment, the method comprising applying a

composition having a drug to a selected portion of the stent, wherein the concentration of the drug in the coating is greater at the middle segment as compared to the first or second end.

70. (New) A method of producing a medicated stent, the stent comprising a first end, an opposing second end, and a middle segment between the two ends, the method comprising depositing a drug along the middle segment of the stent, wherein the two ends are free from any drug.

71. (New) A method of producing a medicated stent, the stent comprising a first end, an opposing second end, and a middle segment between the two ends, the method comprising depositing a drug along the middle segment of the stent, wherein at least one of the two ends has less drug than the middle segment.

72. (New) The method of Claim 71, wherein both ends have less drug than the middle segment.

IN THE ABSTRACT

Please amend the Abstract as indicated below:

A radiation delivery source, such as a stent, and method for making radioactive a delivery source are disclosed. ~~The radiation delivery source has a radioactive region thereon. Radioactivity gradients, located near a proximal end and a distal end of the radioactive region, transition the radioactivity level from a first, therapeutic level to a second, non-therapeutic level. The therapeutic radioactivity level is localized between the radioactivity gradients. The radiation delivery source may be one of many forms, such as stents or source wires. Similarly, a~~A drug delivery source and method for making a drug delivery region on the drug delivery source are also disclosed. ~~A therapeutic concentration of a drug is localized near the central portion of the drug delivery source, such as a drug-eluting balloon catheter or a drug-coated stent. Drug concentration gradients near the proximal and distal ends of the drug delivery region decrease from the therapeutic concentration to a non-therapeutic concentration. The radioactive and drug delivery regions effectively treat intravascular lesions while inhibiting or minimizing cell proliferation near the radioactive and drug delivery ends, a reaction commonly known as the "candy wrapper" effect.~~